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476.10

**TH3 CELLS ARE INDUCED BY ALPHA-MELANOCYTE
STIMULATING HORMONE (α -MSH).**

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Ophthalmology, Harvard Medical School.

The neuropeptide alpha-melanocyte stimulating hormone (α -MSH) is a potent suppressor of inflammation. Recently we have found that α -MSH suppresses IFN- γ production by activated Th1 cells. Although IFN- γ production was suppressed, the T cells continued to proliferate. It has been our goal to characterize the type of effector T cell activity that can be stimulated in the presence of α -MSH. Primed T cells that are TCR-stimulated in the presence of α -MSH proliferate but do not produce IFN- γ nor IL-4; however, they produce significant amounts of TGF- β . These α -MSH-induced, TGF- β -producing T cells are Th3 cells that suppress IFN- γ production by other Th1 cells. This suppression is mediated by TGF- β . Our results indicate that the α -MSH induced Th3 cells are CD4+ CD25+ (IL-2R α) cells. Other laboratories have shown that T cells with this phenotype suppress autoimmunity. Therefore, α -MSH suppresses DTH by mediating a deflection of Th1 into Th3 activity, possibly through expansion of CD25+ primed T cells. The results suggest an important role for α -MSH in mediating and maintaining peripheral tolerance especially in tissues such as the eye and CNS where α -MSH is constitutively expressed. Supported in part by PHS grant EY10752.



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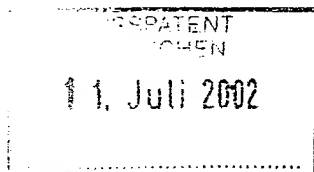
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Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire

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The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





Application Number

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
|---|--|----------------------------------|--|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.7) |
| D,Y | <p>TAYLOR A W ET AL: "Alpha-melanocyte-stimulating hormone suppresses antigen-stimulated T cell production of gamma-interferon." NEUROIMMUNOMODULATION, vol. 1, no. 3, 1994, pages 188-194, XP008005225 ISSN: 1021-7401 * the whole document *</p> <p style="text-align: center;">--- -/--</p> | 1-31 | <p>A01N63/00 C12N5/06 C12N5/08 A61K39/00 A61K35/12 A61K35/14 A61K48/00</p> |
| <p>The supplementary search report has been based on the last set of claims valid and available at the start of the search.</p> | | | <p>TECHNICAL FIELDS SEARCHED (Int.Cl.7)</p> <p>C12N A61K</p> |
| <p>INCOMPLETE SEARCH</p> <p>The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims:</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>Reason for the limitation of the search:</p> <p>see sheet C</p> | | | |
| Place of search | | Date of completion of the search | Examiner |
| THE HAGUE | | 28 June 2002 | Teyssier, B |
| <p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons</p> <p>& : member of the same patent family, corresponding document</p> | | | |



| DOCUMENTS CONSIDERED TO BE RELEVANT | | | CLASSIFICATION OF THE APPLICATION (Int.Cl.7) |
|-------------------------------------|---|-------------------|--|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | |
| D,Y | TAYLOR A W & STREILEN J W: "Alpha-melanocyte stimulating hormone prevents induction of effector T-cell inflammatory activity." FASEB JOURNAL, vol. 10, no. 6, 1996, page A1206 XP002927877 Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists; New Orleans, Louisiana, USA; 2-6 June 1996 ISSN: 0892-6638 Abstract 1194 --- | 1-31 | |
| D,A | LIPTON J M & CATANIA A: "Anti-inflammatory actions of the neuroimmunomodulator alpha-MSH." IMMUNOLOGY TODAY, vol. 18, no. 3, 1997, pages 140-145, XP002902200 ISSN: 0167-5699 --- | | TECHNICAL FIELDS SEARCHED (Int.Cl.7) |
| P,X | TAYLOR A W: "Th3 cells are induced by alpha-melanocyte stimulating hormone (alpha-MSH)." FASEB JOURNAL, vol. 13, no. 4 PART 1, 12 March 1999 (1999-03-12), page A607 XP002203897 Annual Meeting of the Professional Research Scientists for Experimental Biology 99; Washington D.C., USA; 17-21 April 1999 ISSN: 0892-6638 Abstract 476.10 --- -/-- | 1-31 | |



| DOCUMENTS CONSIDERED TO BE RELEVANT | | | CLASSIFICATION OF THE APPLICATION (Int.Cl.7) |
|-------------------------------------|---|-------------------|--|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | |
| T | TAYLOR A W & NAMBA K: "In vitro induction of CD25+ CD4+ regulatory T cells by the neuropeptide alpha-melanocyte stimulating hormone (alpha-MSH)." IMMUNOLOGY AND CELL BIOLOGY, vol. 79, no. 4, August 2001 (2001-08), pages 358-367, XP002203898 ISSN: 0818-9641 ----- | | |
| | | | TECHNICAL FIELDS SEARCHED (Int.Cl.7) |
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European Patent
Office

**INCOMPLETE SEARCH
SHEET C**

Application Number

EP 00 90 9957

Although claims 1-5, to the extent that the method is practised in vivo, and claims 6-19, 24-31 in totality are directed to methods of treatment of the human or animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the composition.